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Executive Progress Report

For

THE MONTE CARLO-BASED DOSIMETRY OF BETA EMITTERS FOR INTRAVASCULAR BRACHYTHERAPY

For the Period of June 1, 1999 through May 31, 2000

Under

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THE MONTE CARLO-BASED DOSIMETRY OF BETA EMITTERS FOR INTRAVASCULAR BACHYTHERAPY (IVBT)

I. Project Description and Objectives

A brachytherapy is a medical treatment with a direct implantation of sealed radioisotope seeds by interstitial, intracavitary, or surface application for non-cancer disease. The use of intravascular sources of radiation (intravascular brachytherapy) is the state-of-the-art radiotherapy modality to inhibit restenosis (reclosure of a blood vessel after angioplasty). Only about ten hospitals in the U.S. are clinically applying intravascular brachytherapy with beta emitters since 1997. Approximately 40% of patients undergoing the interventional coronary procedure (i.e., over 160,000 annually in the United States) have angiographic evidence of restenosis by 12 months, which results in the need for repeated interventional procedure. Even though coronary artery blockage is a nonmalignant disease, the economic impact from this re-procedure in the United States is estimated about $billion per year. Radiation treatment is utilized to reduce the rapid proliferation of cells in the vessel wall. The radiation treatment with beta-particle sources (typically Sr-90 + Y-90) is utilized to prevent restenosis following interventional coronary procedure.

In current clinical trials, the dose calculation is based on either the vendor-provided measurement data or the recommendations by the Radiation Therapy Task Group No. 43 of the American Association of Physicists in Medicine (AAPM), AAPM TG-43. However, these protocols do not properly account for the complicated source geometry (e.g., guide wire, stent, and vessel curvatures) and tissue inhomogeneity. The target site is generally located in a very complicated geometry that consists of both delicate human organs and source delivery components. In addition, there are significant contributions to dose from the secondary radiations such as fluorescent x-rays and atomic electrons. Due to the vicinity between a prescription point and the central line of the seeds being 2 – 3 mm, the measurement of dose variation is not available at this scale. The Monte Carlo method is the only practical solution for difficulties described above; namely, it is highly accurate and intrinsic for inhomogeneity, not subject to any geometrical constrain, and includes all levels of electron/photon transport.

This project aims at developing the Monte Carlo-based dosimetry protocol for accurate calculation of absorbed dose in intravascular brachytherapy using a catheter-based beta-emitter system. The goal of this research is to achieve the accuracy of 5% for brachytherapy dosimetry. The Monte Carlo simulation for the dosimetry and characterization of the catheter-based beta-emitter brachytherapy will be accomplished in five distinct steps as follows in the first year:

Step 1. Simulation of trained sources only in the linear vessel;
Step 2. Simulation of trained sources and a guiding wire in the linear vessel;
Step 3. Simulation of trained sources, a guiding wire, and a stent in the linear vessel;
Step 4. Simulation of trained sources and calcified plaque in the linear vessel; and
Step 5. Simulation of trained sources in the curved vessel.

From these studies, a train effect (dose enhancement due to neighboring seeds) will be investigated, in step by step, increasing the number of the seeds. The contribution of the secondary particles to the dose to a prescription point will be quantitatively estimated as auxiliary metallic devices are introduced.

Experimental studies to verify the Monte Carlo dose calculations for trained beta-sources with and without a guiding wire in the simplified linear vessel model are also planned for the second year.

II. Research Progress for the First Year (June 1, 1999 – May 31, 2000)

1. MCNP Simulation of Trained Sources, a guiding wire, and a stent in Linear Vessel (Steps 1, 2, and 3)

The actual treatment geometry consists of an encapsulated train of seeds, a guide wire, and a stent in a curved vessel. The source is a cylindrical train of 12 source seeds; each having dimensions of 0.64 mm in diameter and 2.5 mm in length, and proximal/distal gold markers. Each seed contains ^{90}Sr/Y mixed with fired ceramic encapsulated in a

0.04 mm stainless steel wall. The Monte Carlo simulations are carried out for the geometry of the train source (including a gold marker) only in the linear vessel with and without a stent. The stent structure is approximately modeled as a set of tori with a rotational radius of 1.92 mm from the source axis and a circular radius of 0.08 mm in cross section. Five tore are equally spaced for each seed. The stent shadows 31% of the total area of the source surface. The MCNP modeling geometry with the resolution of 0.5 mm in axial and trans-axial directions is shown in Fig. 1. The elemental compositions and densities used in the MCNP simulations are described in Table I.

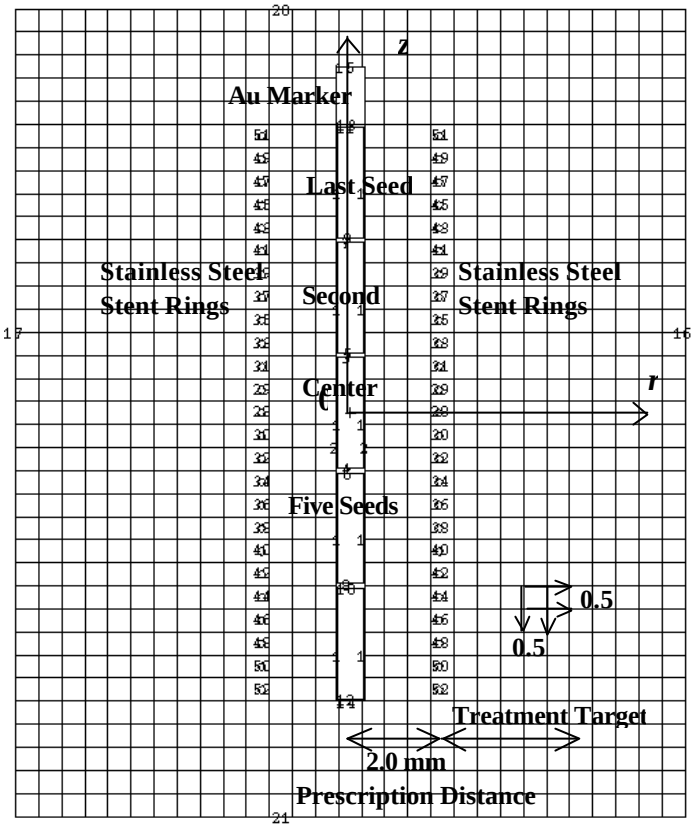

Figure 1. Schematic of the MCNP modeling geometry (2-D) of linear source train with stent. Surrounding water space is composed of 0.5 mm^3-voxels, which are elementary cells for the tallies of dose and flux. The radial distance of 2 mm from the source centerline is the prescription point for intravascular brachytherapy and treatment target is typically located around 2–3 mm beyond that point.

Table I. Elemental compositions and densities of the MCNP simulation geometry.

Materials	Mass Fractions of Composite Elements	Density (g/cm^3)
Source Seed	0.48 Sr, 0.26 O, 0.26 Ti	4.81
Gold Marker	1.0 Au	19.3
Stainless Steel	0.68 Fe, 0.17 Cr, 0.12 Ni, 0.02 Mg, 0.01 Si	7.92
Plaque	0.67 Ca, 0.39 O, 0.04 H	1.45
Water	0.11 H, 0.89 O	1.0

Figure 2 depicts this comparison of radial dose rate distributions (Fig. 2. (a)) at various axial points (see also Fig. 1). Here, the dose distribution of the MCNP simulations was normalized by the total activity of 70 mCi (2.59×10^9 Bq). The dose gradient of the MCNP simulations was very steep, varying from 12 to 0.38 cGy/sec as the radial distance (r) increased from 1.5 to 6.0 mm. The exponential variations are shown in the dose distributions at seeds.

In addition, the agreement between MCNP calculations and the measurements (provided by the vendor) in the region of r = 1.0–3.3 mm was fair (< 5%). Actually, this range corresponds to the region of interest for IVBT. In particular, the MCNP dose rate at r = 2 mm is determined to be 8.38 cGy/sec, which is almost equal to the vendor data (8.4 cGy/sec). However, large deviations appear in the region of r < 1.0 mm or > 3.3 mm. The MCNP calculations show more exponential-like behavior of dose rate than the vendor-provided data. The higher dose of MCNP in r < 1.0 mm would be more reliable considering large potential errors from experimental difficulties at this sub-mm scales, while the higher dose of MCNP in r > 3.3 mm might be less reliable due to the artifacts of MCNP for extremely large Coulomb interactions in low energy (< 10 keV). The electron field at the edge of the last seeds and the gold markers drops gradually along the source axis (z-axis). Since the dose contribution of the neighboring seeds beyond the third seed is negligible (less than 1%), the edge effect is found in the region of the last two seeds and the gold markers. Referring to Fig. 1, the bottom seed does not receive any dose contribution from neighboring seeds below it, while the seed second from the bottom receives the dose contribution only from the bottom seed. Figure 2 (b) depicts the dose perturbation along the axis of the train source (along the axial direction, z, in Fig. 1) at four different radial distances. The doses of the last edge voxels (at z = 5.5–6.0 mm) at each radial distance are less than 60% of the doses of the non-edge voxels (at z < 2 mm). The dose in the region of the gold marker was further reduced; at r = 2 mm, it is only about 40% of the dose of the non-edge voxel. Thus, the treatment length of trained sources is always less than the physical length and, further needs to be defined with considering the edge effect. These were already addressed in the authors' paper (Med. Phys. **27**, 374–380, 2000).

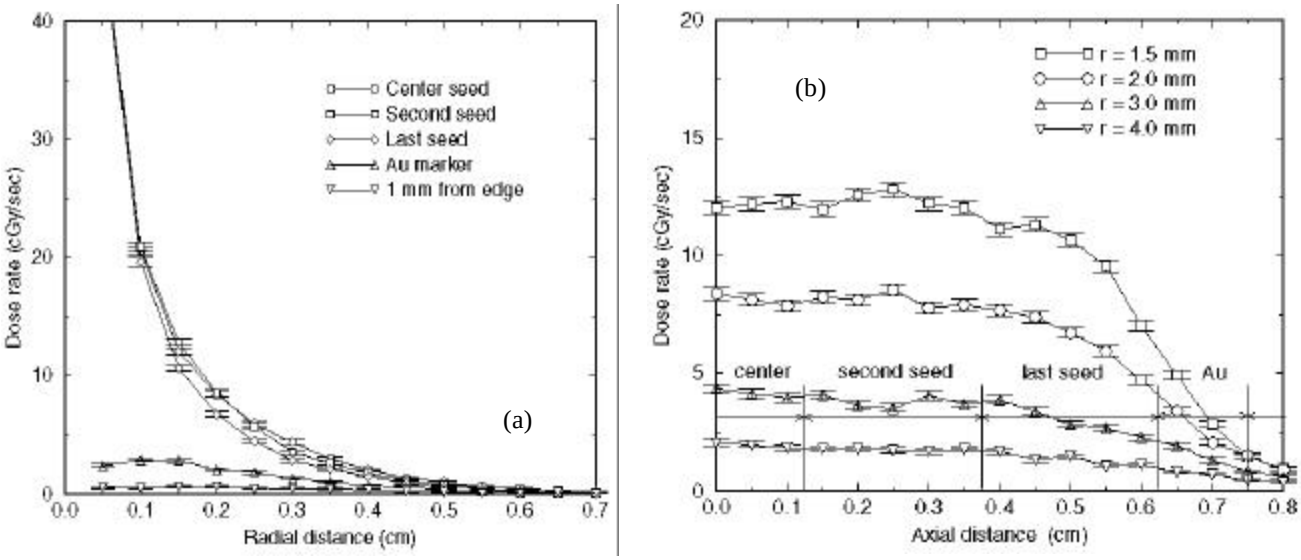

Figure 2. Dose distributions in radial direction (a) at various axial points and in axial direction at various radial distances (see also Fig 1).

2. MCNP Simulation of Trained Sources with Calcified Plaque in Linear Vessel (Step 4)

The calcified plaque is explicitly modeled as a cylindrical wall of 0.5 mm-, 1.0 mm-, or 1.18 mm-thickness (in case of stretching the plaque up to the source) around the vessel (see Fig.3 below). It is known that plaque specimens identified as calcified had an average density of 1.45 g/cm^3. Figure 4 shows the comparison of radial dose distributions beyond the plaque of the three thickness and no plaque. The radial dose distributions decrease with increasing the thickness of a plaque due to the additional attenuation of incoming radiation. In the region of interest (r=0.2 cm – 0.5 cm), the dose reduction with a 0.5 mm-plaque is about 15%, compared to that without plaque, which increases to about 22% with a 1.0 mm-plaque. However, the dose distribution with a 1.18 mm-plaque is almost identical to that with a 1.0 mm-plaque. This implies that, depending on the amount of plaque remained in the vessel (or thickness), the dwelling time of Sr-90/Y-beta source should increase by a factor of the dose reduction to deliver the prescription dose. The effect of calcified plaque on the dose delivery should be more significant for beta-emitters than for gamma-emitters because of a rapid fall-off of beta-dose with the penetration depth.

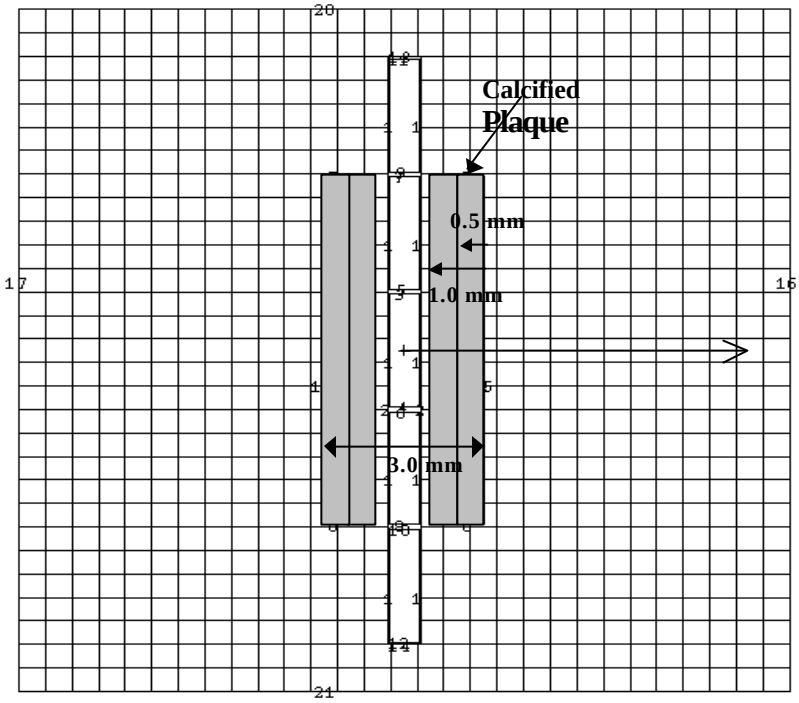

Figure 3. Schematic of the MCNP modeling geometry for calcified plaque around a ^{90}Sr/Y-source train. Calcified plaque is modeled as a cylinder with a thickness of either 0.5 mm or 1.0 mm. If the thickness of a cylindrical plaque is equal to 1.12 mm, then the plaque is contacted with the source train.

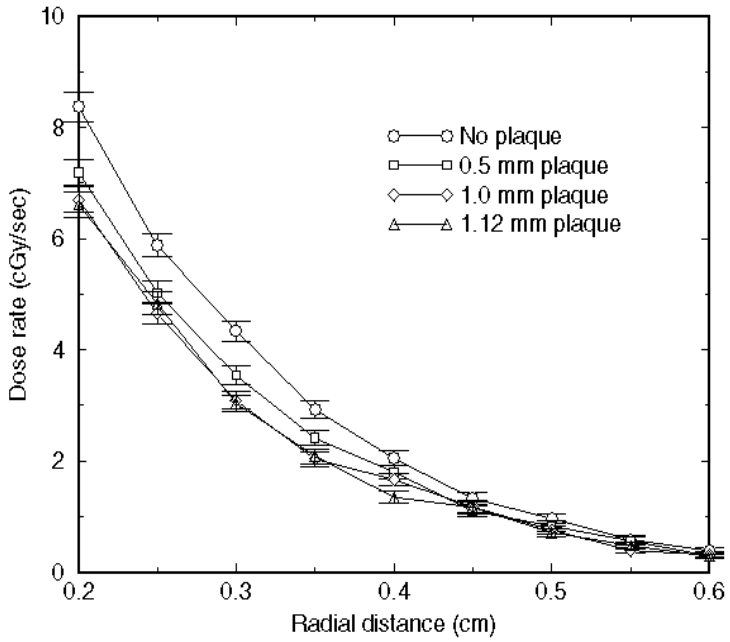

Figure 4. Radial dose distributions for various thickness of calcified plaque described in Fig. 3. A comparison with the dose distribution of no plaque is given. An additional attenuation with calcified plaque is found.

3. MCNP Simulation of Trained Sources in Curved Vessel (Step 5)

The non-uniformity of dose delivery along the coronary artery has been analyzed using Monte Carlo simulations (MCNP). Dosimetric variations along the inside and outside the curvature of seeds have been investigated. Fig. 5 shows the MCNP simulation geometry for the curved source trains, of which the shift angle between neighboring seeds is 5°- or 10°- toward the positive r-direction. Thus, two directions are defined as inward- and outward-curvatures.

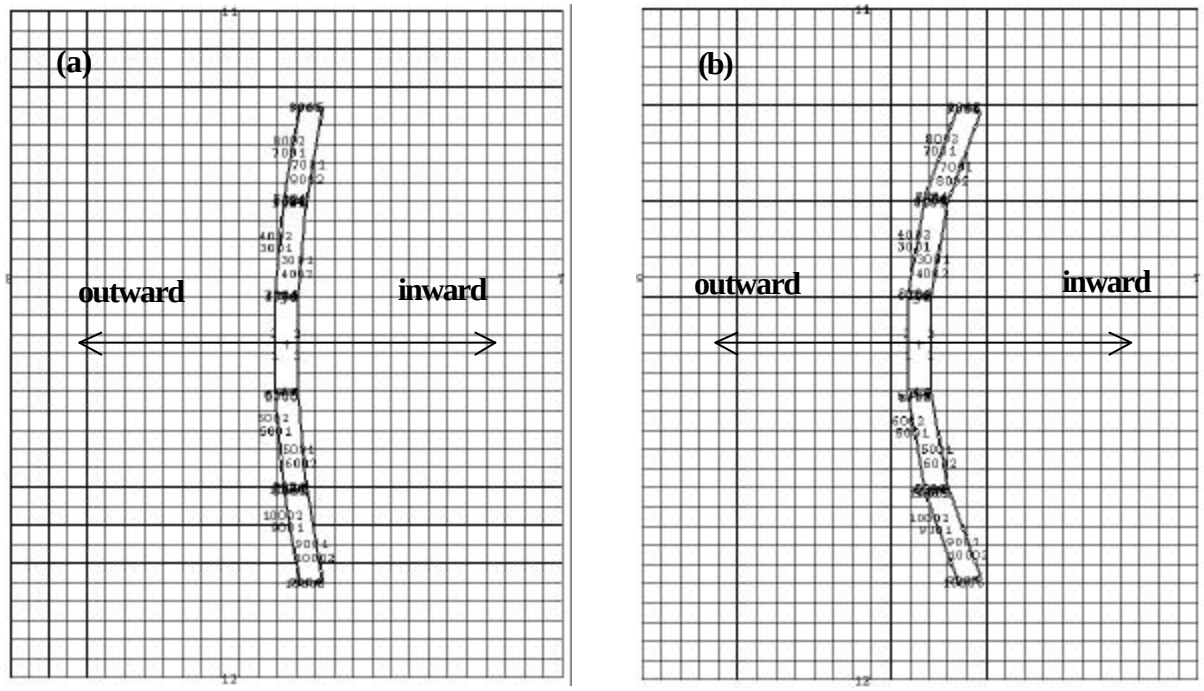

Figure 5. Schematic of the MCNP modeling geometry for curved source trains, of which seeds are consecutively shifted by 5° (a) and 10° (b) with respect to neighboring seeds.

The dose in voxels of Fig. 5 was normalized by the total activity of 70mCi (2.59×10^9 Bq). Fig. 6 shows radial dose variation in inward-curvature (a) and outward-curvature (b) directions for both 5- and 10-degrees shifted vessels. As seen in Fig. 6, dose increase in inward-curvature and dose reduction in the outward-curvature increase with increasing angle shifted between neighboring seeds. The degree of increase and reduction in 5-degree-shifted vessel is around 4% at the prescription point (r = 2 mm). However, to achieve the accuracy of 5% in dosimetry of radiotherapy, the variation by small degree of curvature (~5 degree) also should be taken into account for dosimetry planning. In the 10-degree shifted vessel, the dose rates increased around 8% at the prescription point. Therefore, hot and cold areas will be found because of partially high degree of curvature in coronary artery. As radial distance increases beyond r = 3 mm, the degree of increase in inward curvature is likely to be increased, while the degree of reduction in outward curvature is not significant. This is due to a very short range of betas in water (4 mm for 1 MeV electrons).

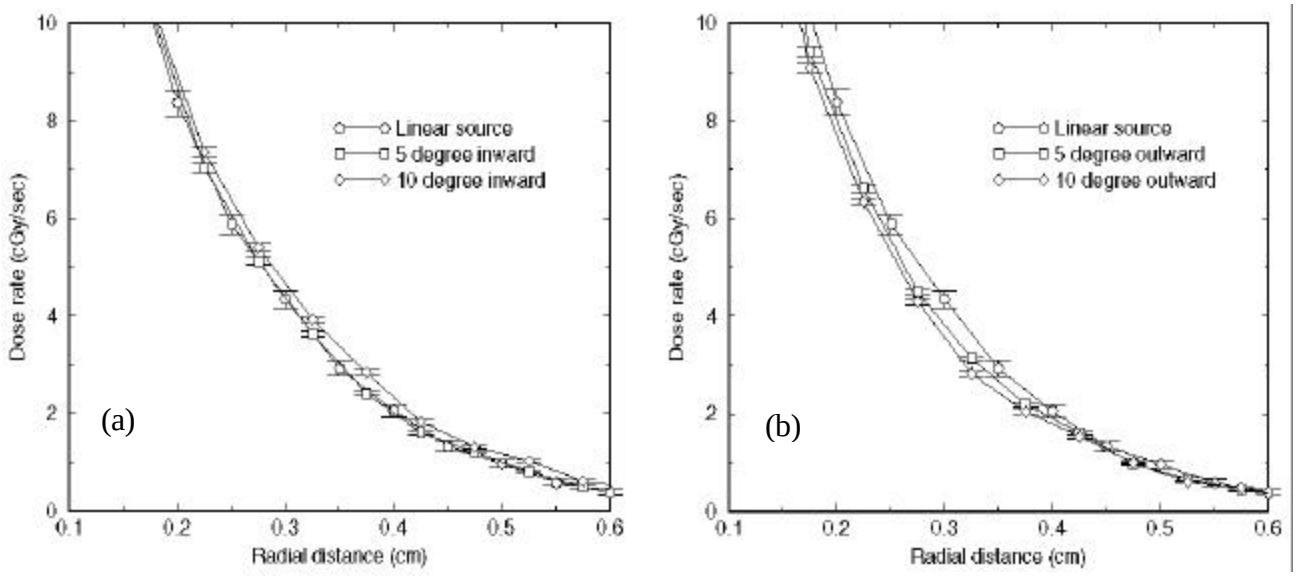

Figure 6. Radial dose distributions for inward- (a) and outward- (b) directions of the two curved source trains. The comparison with the radial dose distribution of the linear source is given.

III. Experimental Set-Ups for the Second Year (June 1, 2000 – May 31, 2001)

Progress is underway for the experimental studies to verify the Monte Carlo dose calculations. Radiochromic film, solid water phantom, densitometer with PC, etc. have all been acquired and the equipments are presently being calibrated. This progress is consistent with the schedule for Year-2 of the proposed study.

IV. Summary and Accomplishments

During the current project period, June 1, 1999 through May 31, 2000, the project has achieved its original goal as proposed in the milestone chart within the proposed budget. The Monte Carlo-based simulations for linear and curved vessels with and without stent and also calcified plaque have been developed. The simulations indicate that the presence of metallic stent and the calcified plaque alter significantly the actual dose in the treatment areas. The vessel curvature effect did not appear profound initially, however, the relative difference of the radial dose appeared to be as much as 20% and 40% for the outwardly and inwardly curvatured seeds, respectively. Experimental verifications for these MCNP simulations will follow in the second phase in Year-2 during June 1, 2000 through May 31, 2001.